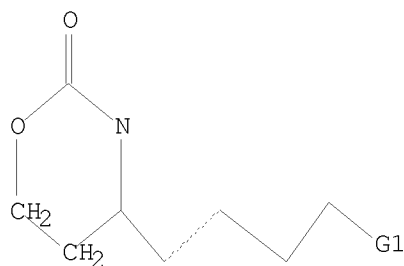


L1 STR



G1 Ak,Cy

Structure attributes must be viewed using STN Express query preparation.

=&gt; s l1

SAMPLE SEARCH INITIATED 16:13:41 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 27 TO ITERATE

100.0% PROCESSED 27 ITERATIONS

4 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 229 TO 851

PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

=&gt; s l1 sss full

FULL SEARCH INITIATED 16:13:51 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 335 TO ITERATE

100.0% PROCESSED 335 ITERATIONS

81 ANSWERS

SEARCH TIME: 00.00.01

L3 81 SEA SSS FUL L1

=&gt; file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

178.36

178.57

FILE 'CAPLUS' ENTERED AT 16:13:55 ON 19 MAY 2008

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FILE LAST UPDATED: 18 May 2008 (20080518/ED)

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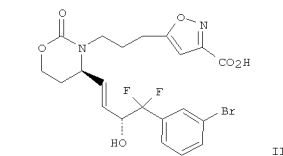
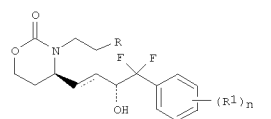
L4 9 L3

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L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2007:144056 CAPLUS  
 DOCUMENT NUMBER: 146:229363  
 TITLE: Preparation of oxazine derivatives as Ep4 receptor agonists and antiglaucoma agents  
 INVENTOR(S): Colucci, John; Han, Yongxin; Farand, Julie A.  
 PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.  
 SOURCE: PCT Int. Appl., 54pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014462	A1	20070208	WO 2006-CA1254	20060728
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW</p> <p>RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>AU 2006275263 A1 20070208 AU 2006-275263 20060728            CA 2616608 A1 20070208 CA 2006-2616608 20060728            EP 1912957 A1 20080423 EP 2006-761199 20060728</p> <p>R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR</p> <p>PRIORITY APPLN. INFO.: US 2005-705120P P 20050803</p> <p>WO 2006-CA1254 W 20060728</p>				
<p>OTHER SOURCE(S): MARPAT 146:229363            GI</p>				

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



AB This invention relates to potent selective agonists of the EP4 subtype of prostaglandin E2 receptors 1, wherein R represents (CH2)<sub>n</sub>COOR<sub>3</sub>, (CH2)<sub>n</sub>C3-10 cycloalkyl, -(CH2)<sub>n</sub>C3-10 heterocyclyl, (CH2)<sub>n</sub>C5-10 aryl, said cycloalkyl, heterocyclyl, and aryl substituted with R<sub>2</sub>; provided that

when R is -(CH2)<sub>n</sub>C3-10 heterocyclyl it does not represent thienyl; R<sub>1</sub> independently represents hydrogen, Cl-6-alkyl, halogen, CF<sub>3</sub>, aryl, said aryl optionally substituted with 1-3 groups of halogen, Cl-6 alkyl, CF<sub>3</sub>, or N(R<sub>4</sub>)<sub>2</sub>; R<sub>2</sub> represents COOR<sub>3</sub> or a carboxylic acid isostere; R<sub>3</sub> and R<sub>4</sub> independently represent H, or Cl-6-alkyl; n represents 0-3; x is 2-5, their use or a formulation thereof in the treatment of glaucoma and other conditions, which are related to elevated intraocular pressure in the eye of a patient. This invention further relates to the use of the compds.

of this invention for mediating the bone modeling and remodeling processes of the osteoblasts and osteoclasts. Thus, oxazine II was prepared and tested in rats as Ep4 receptor agonist in osteoblastic cell lines and in bone tissue. Effects of an EP4 agonist on intraocular pressure in rabbits and monkeys, are reported. Title compds. showed improved ocular tolerability in animal species such as rabbits and cynomolgus monkeys. The activity range of the compds. of this invention for bone use is between 0.01 and 100,000 nM. Stable expression of prostanoid receptors in the human embryonic kidney (HEK) 293 (EBNA) cell line is reported.

IT 924622-95-7P 924622-97-9P 924622-99-1P  
 924623-02-9P 924623-03-0P 924623-05-2P  
 924623-06-3P 924623-07-4P 924623-08-5P  
 924623-09-6P 924623-11-0P 924623-12-1P

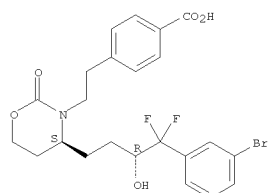
L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

924623-13-2P 924623-14-3P 924623-15-4P  
 924623-16-5P 924623-17-6P 924623-18-7P  
 924623-19-8P 924628-52-4P 924628-53-5P  
 RI: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of oxazine derivs. as Ep4 receptor agonists antiglaucoma agents)

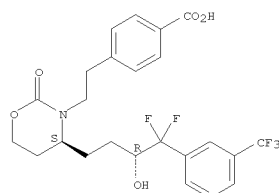
RN 924622-95-7 CAPLUS  
 CN Benzoic acid, 4-[2-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 924622-97-9 CAPLUS  
 CN Benzoic acid, 4-[2-[(4S)-4-[(3R)-4,4-difluoro-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



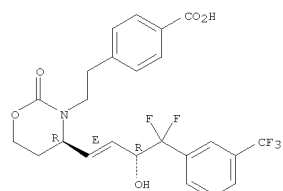
RN 924622-99-1 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)- (CA INDEX NAME)

Habte

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

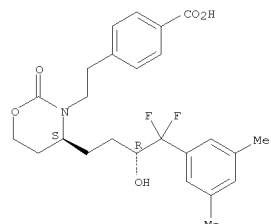
yl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-02-9 CAPLUS  
 CN Benzoic acid, 4-[2-[(4S)-4-[(3R)-4-(3,5-dimethylphenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.

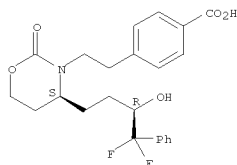


RN 924623-03-0 CAPLUS  
 CN Benzoic acid, 4-[2-[(4S)-4-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.

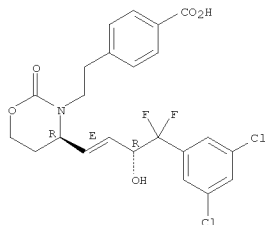
05/19/2008

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-05-2 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3,5-dichlorophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

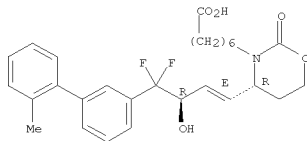


RN 924623-06-3 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

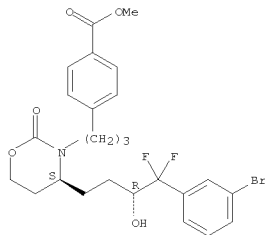
L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-11-0 CAPLUS  
 CN Benzoic acid, 4-[3-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, methyl ester (CA INDEX NAME)

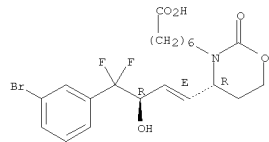
Absolute stereochemistry.



RN 924623-12-1 CAPLUS  
 CN Benzoic acid, 4-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

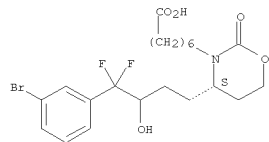
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



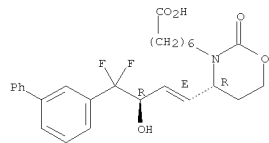
RN 924623-07-4 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



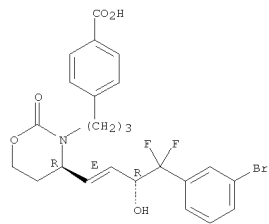
RN 924623-08-5 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4-[1,1'-biphenyl]-3-yl-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



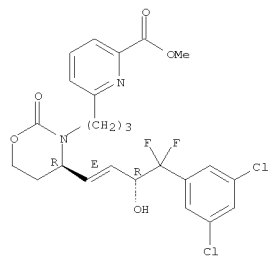
RN 924623-09-6 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-13-2 CAPLUS  
 CN 2-Pyridinecarboxylic acid, 6-[3-[(4R)-4-[(1E,3R)-4-(3,5-dichlorophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, methyl ester (CA INDEX NAME)

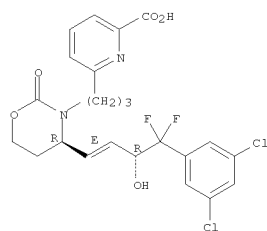
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-14-3 CAPLUS  
 CN 2-Pyridinecarboxylic acid, 6-[3-[(4R)-4-[(1E,3R)-4-(3,5-dichlorophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

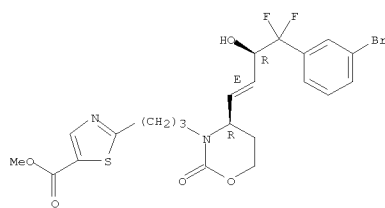
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-15-4 CAPLUS  
 CN 5-Thiazolecarboxylic acid, 2-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, methyl ester (CA INDEX NAME)

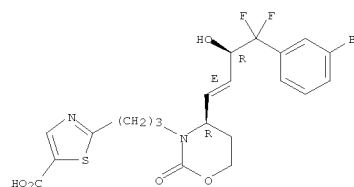
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-16-5 CAPLUS  
 CN 5-Thiazolecarboxylic acid, 2-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

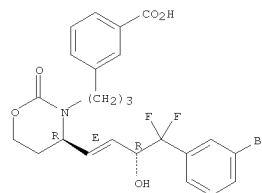
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-17-6 CAPLUS  
 CN Benzoic acid, 3-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

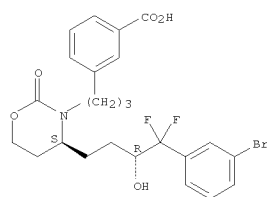
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-18-7 CAPLUS  
 CN Benzoic acid, 3-[3-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

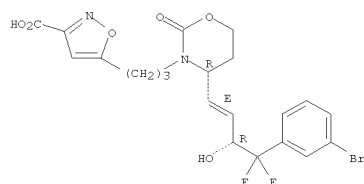
Absolute stereochemistry.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-19-8 CAPLUS  
 CN 3-Isoxazolecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

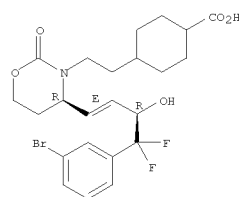
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924628-52-4 CAPLUS  
 CN Cyclohexanecarboxylic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

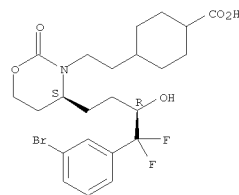
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924628-53-5 CAPLUS  
 CN Cyclohexanecarboxylic acid, 4-[2-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]- (CA INDEX NAME)

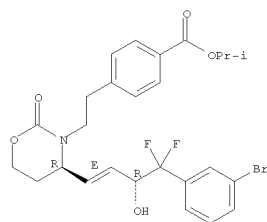
Absolute stereochemistry.



IT 924622-92-4P 924622-93-5P 924622-94-6P  
 924622-96-8P 924622-98-0P 924623-00-7P  
 924623-01-8P 924623-04-1P 924623-10-9P  
 924623-27-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of oxazine derivs. as Ep4 receptor agonists antiglaucoma agents)  
 RN 924622-92-4 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

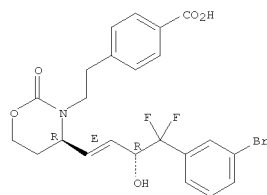
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924622-93-5 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

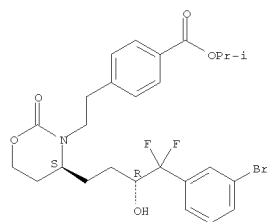
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924622-94-6 CAPLUS  
 CN Benzoic acid, 4-[2-[(4S)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

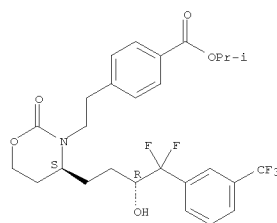
Absolute stereochemistry.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924622-96-8 CAPLUS  
 CN Benzoic acid, 4-[2-[(4S)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

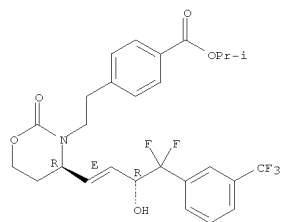
Absolute stereochemistry.



RN 924622-98-0 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

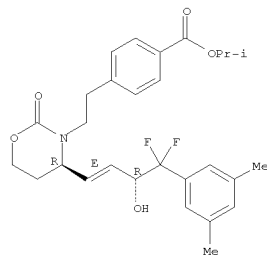
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-00-7 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3,5-dimethylphenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

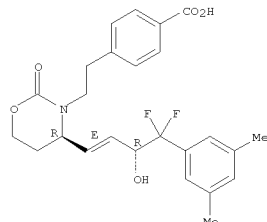
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-01-8 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3,5-dimethylphenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

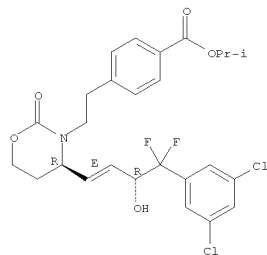
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-04-1 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3,5-dichlorophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

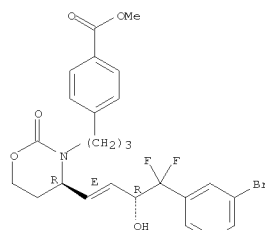
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924623-10-9 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

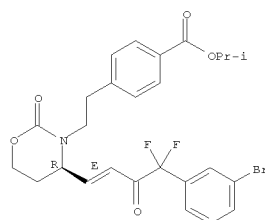
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924623-27-8 CAPLUS  
 CN Benzoic acid, 4-[2-[(4R)-4-[(1E)-4-(3-bromophenyl)-4,4-difluoro-3-oxo-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]ethyl]-, 1-methylethyl ester (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

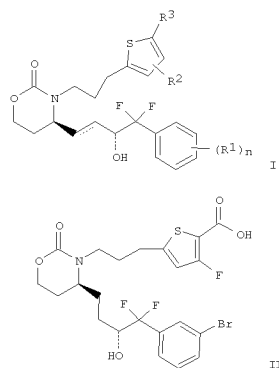
L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:143969 CAPLUS  
 DOCUMENT NUMBER: 146:229362  
 TITLE: Preparation of oxazine derivatives as Ep4 receptor agonists and antiglaucoma agents  
 INVENTOR(S): Colucci, John; Han, Yongxin; Farand, Julie A.  
 PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.  
 SOURCE: PCT Int. Appl., 47pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014454	A1	20070208	WO 2006-CA1243	20060728
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2006275270	A1	20070208	AU 2006-275270	20060728
CA 2616604	A1	20070208	CA 2006-2616604	20060728
EP 1912977	A1	20080423	EP 2006-761196	20060728
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRIORITY APPLN. INFO.:			US 2005-705124P	P 20050803
			WO 2006-CA1243	W 20060728

OTHER SOURCE(S): MARPAT 146:229362  
 GI

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



AB This invention relates to potent selective agonists of the EP4 subtype of prostaglandin E2 receptors 1, wherein R1 independently represents hydrogen, C1-6 alkyl, halogen, CF3, aryl, said aryl optionally substituted

with 1 to 3 groups of halogen, C1-6 alkyl, CF3, substituted amine; R2 represents H, or halogen; R3 represents COOR or carboxylic acid isostere; n represents 0-3; their use or a formulation thereof in the treatment of glaucoma and other conditions, which are related to elevated intraocular pressure in the eye of a patient. This invention further relates to the use of the compds. of this invention for mediating the bone modeling and remodeling processes of the osteoblasts and osteoclasts. Thus, oxazine

was prepared and tested in rats as EP4 receptor agonist in osteoblastic

cell lines and in bone tissue. Effects of an EP4 agonist on intraocular pressure in rabbits and monkeys, are reported. Title compds. showed improved ocular tolerability in animal species such as rabbits and cynomolgus monkeys.

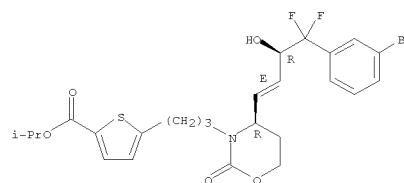
IT 924300-94-7P 924300-95-8P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of oxazine derivs. as EP4 receptor agonists and antiglaucoma agents)

RN 924300-94-7 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-

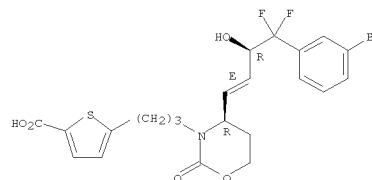
L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924300-95-8 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



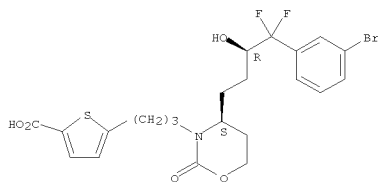
IT 924300-96-9P 924300-98-1P 924301-00-8P  
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 924301-08-6P 924301-09-7P 924301-11-1P  
 924301-12-2P 924301-13-3P 924301-15-5P  
 924301-37-1P 924301-38-2P 924301-39-3P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of oxazine derivs. as EP4 receptor agonists and antiglaucoma agents)

RN 924300-96-9 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA

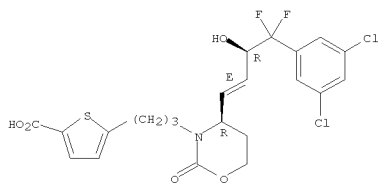
L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
INDEX NAME

Absolute stereochemistry.



RN 924300-98-1 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3,5-dichlorophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

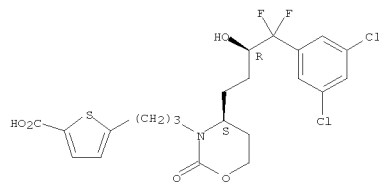
Absolute stereochemistry.  
Double bond geometry as shown.



RN 924301-00-8 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4-(3,5-dichlorophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

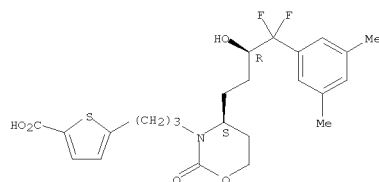
Absolute stereochemistry.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-03-1 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4-(3,5-dimethylphenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

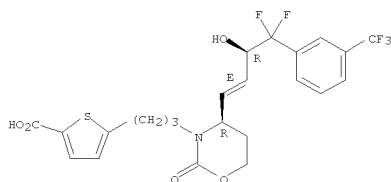
Absolute stereochemistry.



RN 924301-05-3 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3,5-difluoro-3-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

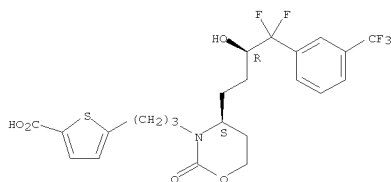
Absolute stereochemistry.  
Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-07-5 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4,4-difluoro-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

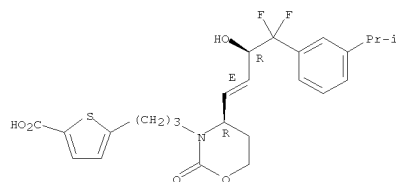
Absolute stereochemistry.



RN 924301-08-6 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-[3-(1-methylethyl)phenyl]-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

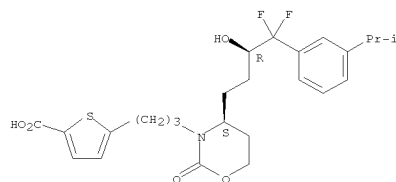
Absolute stereochemistry.  
Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-09-7 CAPLUS  
CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4,4-difluoro-3-hydroxy-4-[3-(1-methylethyl)phenyl]butyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

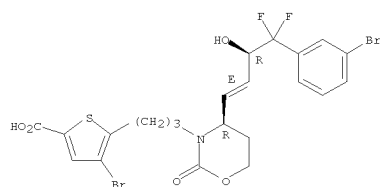
Absolute stereochemistry.



RN 924301-11-1 CAPLUS  
CN 2-Thiophenecarboxylic acid, 4-bromo-5-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

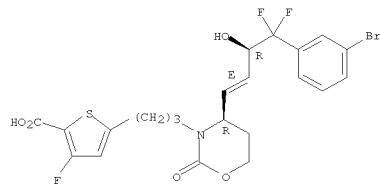
Absolute stereochemistry.  
Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-12-2 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-3-fluoro- (CA INDEX NAME)

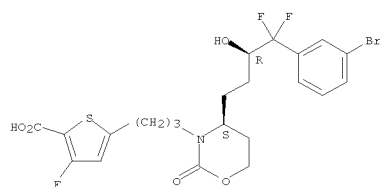
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924301-13-3 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-3-fluoro- (CA INDEX NAME)

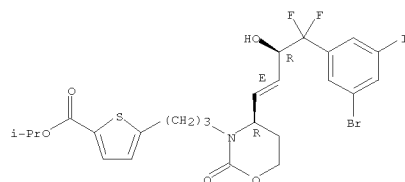
Absolute stereochemistry.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-15-5 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3-bromo-5-iodophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

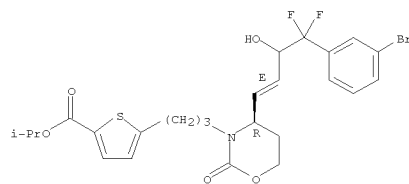
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924301-37-1 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

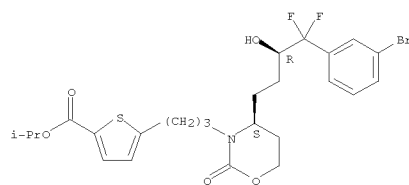
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-38-2 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4-(3-bromophenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

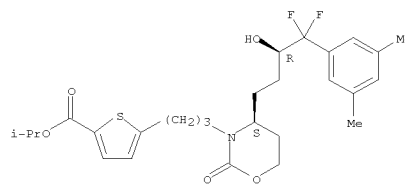
Absolute stereochemistry.



RN 924301-39-3 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4S)-4-[(3R)-4-(3,5-dimethylphenyl)-4,4-difluoro-3-hydroxybutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

Absolute stereochemistry.

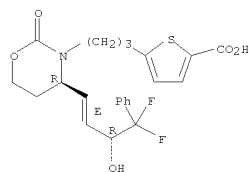
L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



IT 768400-29-9P 924300-97-0P 924300-99-2P  
 924301-01-9P 924301-02-0P 924301-04-2P  
 924301-06-4P 924301-10-0P 924301-21-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of oxazine derivs. as EP4 receptor agonists and antiglaucoma agents)

RN 768400-29-9 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

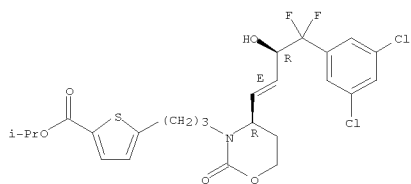
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924300-97-0 CAPLUS  
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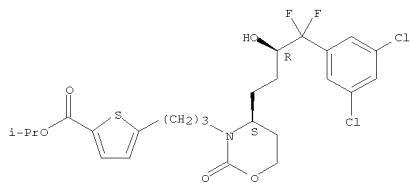
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924300-99-2 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4S)-4-[(3R)-4-(3,5-dichlorophenyl)-4,4-  
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 1-methylethyl ester (CA INDEX NAME)

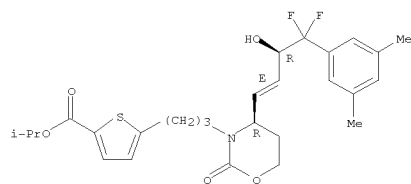
Absolute stereochemistry.



RN 924301-01-9 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3,5-dimethylphenyl)-  
 4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-  
 yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

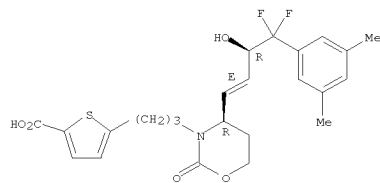
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-02-0 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E,3R)-4-(3,5-dimethylphenyl)-  
 4,4-difluoro-3-hydroxy-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-  
 yl]propyl]- (CA INDEX NAME)

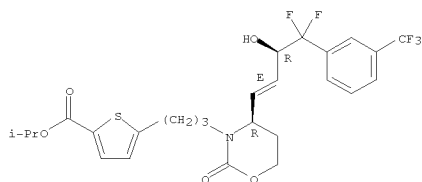
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 924301-04-2 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-  
 [3-(trifluoromethyl)phenyl]-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-  
 yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

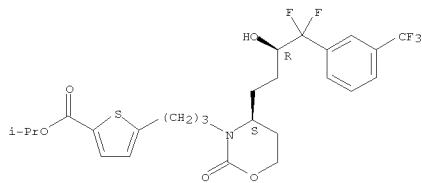
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 924301-06-4 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4S)-4-[(3R)-4,4-difluoro-3-hydroxy-4-[3-  
 (trifluoromethyl)phenyl]butyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-,  
 1-methylethyl ester (CA INDEX NAME)

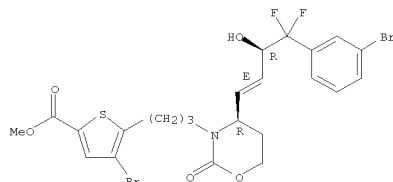
Absolute stereochemistry.



RN 924301-10-0 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 4-bromo-5-[3-[(4R)-4-[(1E,3R)-4-(3-  
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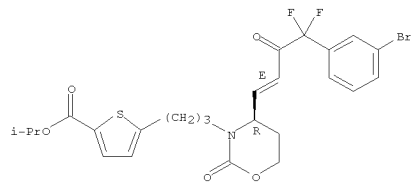
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



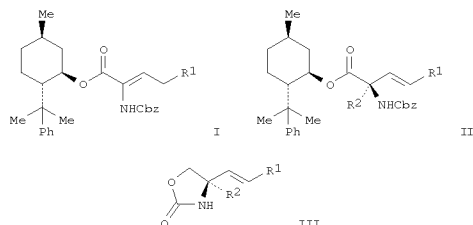
RN 924301-21-3 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-4-[(1E)-4-(3-bromophenyl)-4,4-  
 difluoro-3-oxo-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-,  
 1-methylethyl ester (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:1136535 CAPLUS  
 DOCUMENT NUMBER: 146:100991  
 TITLE: Efficient Asymmetric Synthesis of Quaternary  
 (E)-Vinylglycines by Deconjugative Alkylation of  
 Dehydroamino Acids  
 AUTHOR(S): Jones, Matthew C.; Marsden, Stephen P.; Subtil, Dulce  
 M. Munoz  
 CORPORATE SOURCE: School of Chemistry, University of Leeds, Leeds, LS2  
 9JT, UK  
 SOURCE: Organic Letters (2006), 8(24), 5509-5512  
 CODEN: ORLEF7; ISSN: 1523-7060  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 146:100991  
 GI

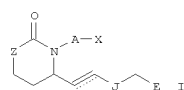


AB A two-step protocol for the asym. synthesis of protected quaternary  
 (E)-vinylglycines from simple aldehydes is reported. The key step is a  
 regiocontrolled deconjugative asym. alkylation of dehydroamino acids,  
 such that the target compds. are produced as single geometric isomers with  
 high diastereoselectivity. For example, dehydroamino acid I (R1 = C8H17, Ph,  
 CH2Ph) are alkylated in presence of LDA, LiCl in THF to give  
 vinylglycines II (R2 = Me, Et, CH2Ph, CH2CH=CH2, CH2OCH2Ph, CH2CO2Bu-t) in yields  
 ≥33% with 92-96% diastereomeric excess. II can be converted to  
 protected quaternary β-amino alcs., oxazolidinones III, by  
 chemoselective reduction  
 IT 917603-84-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (asym. preparation of quaternary vinylglycines by deconjugative  
 alkylation)

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:116566 CAPLUS  
 DOCUMENT NUMBER: 144:192030  
 TITLE: Preparation of prostaglandin analogs as antiglaucoma  
 agents  
 INVENTOR(S): Old, David W.; Dinh, Danny T.  
 PATENT ASSIGNEE(S): Allergan, Inc., USA  
 SOURCE: PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006014207	A1	20060209	WO 2005-US19409	20050602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005270230	A1	20060209	AU 2005-270230	20050602
CA 2571786	A1	20060209	CA 2005-2571786	20050602
EP 1771427	A1	20070411	EP 2005-761544	20050602
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20060276461	A1	20061207	US 2005-552083	20051004
PRIORITY APPLN. INFO.:			US 2004-584962P	P 20040702
			US 2004-600165P	P 20040809
			WO 2005-US19409	W 20050602

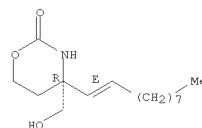
OTHER SOURCE(S): MARPAT 144:192030  
 GI



AB Compds. of formula I [A = (CH2)6, cis-CH2CH=CH(CH2)3, CH2C.tplbond.C(CH2)3;  
 Z = O, S, (substituted) NH; X = CO2H, (substituted) CONH2, etc.; J = CO,  
 GI

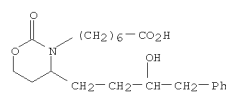
L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
 of dehydroamino acids)  
 RN 917603-84-0 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 4-(1E)-1-decen-1-yltetrahydro-4-(hydroxymethyl)-,  
 (4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

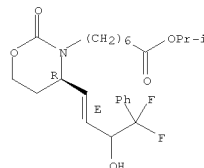
L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
 CHOH; E = alkyl, cycloalkyl, Ph, naphthyl or a pharmaceutically  
 acceptable salt or a produg thereof is disclosed herein. These compds.  
 are useful for treating glaucoma or ocular hypertension.  
 IT 875314-81-1DP, derivs.  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of prostaglandin analogs as antiglaucoma agents)  
 RN 875314-81-1 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid,  
 dihydro-4-(3-hydroxy-4-phenylbutyl)-2-  
 oxo- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

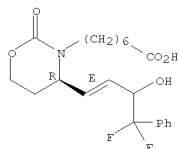
L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
 PREPARATION; RACT (Reactant or reagent); USES (Uses)  
 (drug candidate; prepn. of disubstituted piperidinones, oxazinanones, thiazinanones, and morpholinones as EP4 receptor agonists for treatment of ocular and bone disorders)  
 RN 768399-98-0 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
 PREPARATION; RACT (Reactant or reagent); USES (Uses)  
 (drug candidate; prepn. of disubstituted piperidinones, oxazinanones, thiazinanones, and morpholinones as EP4 receptor agonists for treatment of ocular and bone disorders)  
 RN 768399-98-0 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.

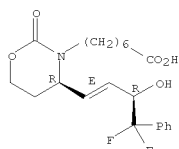


IT 768399-99-1P 768400-11-9P, 7-[(4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-2-oxo-1,3-oxazin-3-yl]heptanoic acid 768400-14-2P, 7-[(4S)-4-((3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl)-2-oxo-1,3-oxazin-3-yl]heptanoic acid 768400-18-6P, Isopropyl 7-[(4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-2-oxo-1,3-oxazin-3-yl]heptanoate 768400-21-1P, (4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-3-[6-(2H-tetraazol-5-yl)hexyl]-1,3-oxazin-2-one 768400-29-9P, 5-[3-[(4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-2-oxo-1,3-oxazin-3-yl]propyl]thiophene-2-carboxylic acid 768400-32-4P, (4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-3-[3-[5-(2H-tetraazol-5-yl)thien-2-yl]propyl]-1,3-oxazin-2-one 768400-35-7P, (4S)-4-((3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl)-3-[3-[5-(2H-tetraazol-5-yl)thien-2-yl]propyl]-1,3-oxazin-2-one 768400-40-4P, Isopropyl 5-[3-[(4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-2-oxo-1,3-oxazin-3-yl]propyl]thiophene-2-carboxylate 866465-52-3P, (5E)-7-[(4R)-4-((1E,3R)-4,4-difluoro-3-hydroxy-4-phenylbut-1-enyl)-2-oxo-1,3-oxazin-3-yl]hept-5-enoic acid 866465-55-6P, (5E)-7-[(4S)-4-((3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl)-2-oxo-1,3-oxazin-3-yl]hept-5-enoic acid  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
 (drug candidate; prepn. of disubstituted piperidinones, oxazinanones, thiazinanones, and morpholinones as EP4 receptor agonists for treatment of ocular and bone disorders)  
 RN 768399-99-1 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.

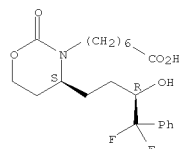


RN 768400-11-9 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.

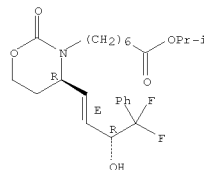


RN 768400-14-2 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]dihydro-2-oxo-, (4S)- (CA INDEX NAME)  
 Absolute stereochemistry.

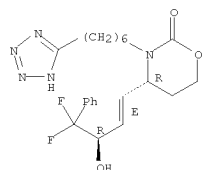
L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 768400-18-6 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.

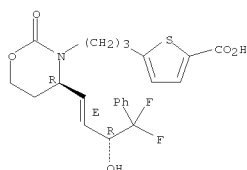


RN 768400-21-1 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]tetrahydro-3-[6-(2H-tetraazol-5-yl)hexyl]-, (4R)- (CA INDEX NAME)  
 Absolute stereochemistry.  
 Double bond geometry as shown.



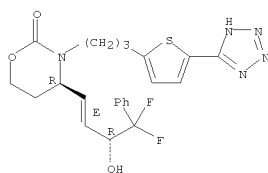
L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)  
 RN 768400-29-9 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



RN 768400-32-4 CAPLUS  
 CN 2H-1,3-Oxazin-2-one,  
 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]tetrahydro-3-[3-[5-(2H-tetrazol-5-yl)-2-thienyl]propyl]-, (4R)- (CA INDEX NAME)

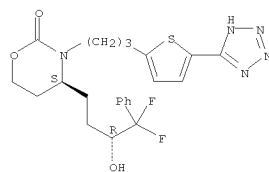
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 768400-35-7 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 4-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]tetrahydro-3-[3-[5-(2H-tetrazol-5-yl)-2-thienyl]propyl]-, (4S)- (CA INDEX NAME)

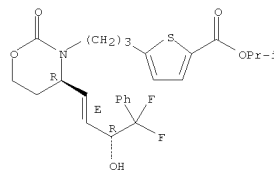
Absolute stereochemistry.

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 768400-40-4 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

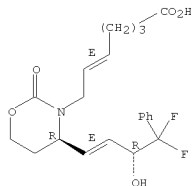
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 866465-52-3 CAPLUS  
 CN 5-Heptenoic acid, 7-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]-, (5E)-rel- (CA INDEX NAME)

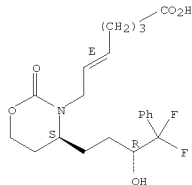
Relative stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 866465-55-6 CAPLUS  
 CN 5-Heptenoic acid, 7-[(4R)-4-[(3S)-4,4-difluoro-3-hydroxy-4-phenylbutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]-, (5E)-rel- (CA INDEX NAME)

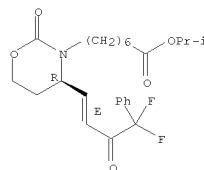
Relative stereochemistry.  
 Double bond geometry as shown.



IT 768400-09-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of disubstituted piperidinones, oxazinanones, thiazinanones, and morpholinones as EP4 receptor agonists for treatment of ocular and bone disorders)  
 RN 768400-09-5 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid,  
 4-[(1E)-4,4-difluoro-3-oxo-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

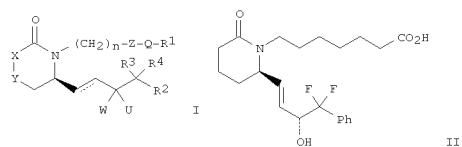
L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS ON STN  
ACCESSION NUMBER: 2004:817887 CAPLUS  
DOCUMENT NUMBER: 141:314052  
TITLE: Preparation of prostaglandin analogs as EP4 receptor  
agonists for the treatment of glaucoma  
INVENTOR(S): Billot, Xavier; Colucci, John; Han, Yongxin; Wilson,  
Marie-claire; Young, Robert M.  
PATENT ASSIGNEE(S): Merck Frost Canada & Co., Can.  
SOURCE: PCT Int. Appl., 69 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
PATENT ACC. NUM. COUNT: 2  
PATENT INFORMATION:

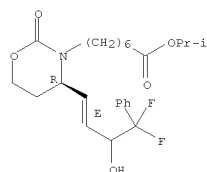
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085430	A1	20041007	WO 2004-CA470	20040326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NA, NI, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MG, MN, MZ, SD, SL, SZ, TZ, ZM, ZW, AM, AZ, ES, FI, FR, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, EG, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004224261	A1	20041007	AU 2004-224261	20040326
CA 2519938	A1	20041007	CA 2004-2519938	20040326
WO 2004085431	A1	20041007	WO 2004-CA471	20040326
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RW: BW, GH, GM, KE, LS, MG, MN, MZ, SD, SL, SZ, TZ, ZM, ZW, AM, AZ, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1713621	A1	20060111	EP 2004-723484	20040326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LT, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004080690	A	20060328	BR 2004-8690	20040326
CN 1746593	A	20060626	CN 2004-80008186	20040326
JP 2006520758	T	20060914	JP 2006-504019	20040326
US 2005DN03925	A	20070824	US 2005-DN3925	20050902
US 2005DN03928	A	20070824	US 2005-DN3928	20050902
MX 2005PA10189	A	20060222	MX 2005-PA10189	20050923
NO 20050504951	A	20051222	NO 2005-4951	20051025
PRIORITY APPLN. INFO.			US 2003-457700P	P 20030326



AB	Prostaglandin analogs of formula I (Q = alkylene, alkarylene, alkylycloalkylene, etc.; X, Y = CH <sub>2</sub> , O, (substituted) NH, S; U = H, alkyl, absent; W = OH, oxo; R <sub>1</sub> = hydroxyalkyl, cyanoalkyl, carboxy, heterocyclylalkyl, etc.; R <sub>2</sub> = alkyl, aryl, heteroaryl, etc.; R <sub>3</sub> , R <sub>4</sub> = H, halo, alkyl; R <sub>3</sub> R <sub>4</sub> = alkylene, etc.; Z = triple bond, O, S, CH=CH, etc.; n = 0-4) are prepared as potent selective agonists of the EP <sub>4</sub> subtype of prostaglandin E <sub>2</sub> receptors, and can be used in a formulation for the treatment of glaucoma and other conditions, which are related to elevated intraocular pressure in the eye of a patient. This invention further relates to the use of the compds. of this invention for mediating the remodeling and remodeling processes of the osteoblasts and osteoclasts.
bone	
IT	Thus, II was prepared in several steps from (R)-pipecolic acid. 768299-98-0 R <sub>1</sub> : PAC (Pharmacological activity); R <sub>2</sub> : RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of prostaglandin analogs as EP <sub>4</sub> receptor agonists for the treatment of glaucoma)
RN	768299-98-0 CAPLUS
CN	2H-1,3-Oxazine-3(H)-heptanoic acid, 4-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)

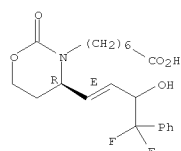
Absolute stereochemistry.  
Double bond geometry as shown.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



IT	768399-99-1P	768400-11-9P	768400-14-2P
	768400-16-4P	768400-18-6P	768400-21-1P
	768400-26-6P	768400-29-9P	768400-32-4P
	768400-35-7P	768400-37-9P	768400-40-4P
	768400-43-7P	768400-46-0P	
	RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of prostaglandin analogs as EP4 receptor agonists for the treatment of glaucoma)		
RN	768399-99-1	CAPLUS	
	2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E)-4,4-difluoro-3-hydroxy-4- phenyl-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)		

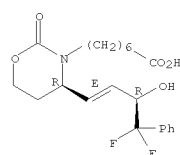
Absolute stereochemistry.  
Double bond geometry as shown.



RN 768400-11-9 CAPLUS  
CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, (4R)- (CA INDEX NAME)

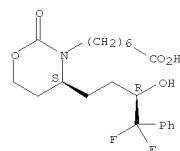
Absolute stereochemistry.  
Double bond geometry as shown.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



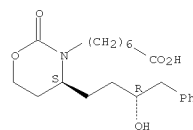
RN 768400-14-2 CAPLUS  
CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]dihydro-2-oxo-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 768400-16-4 CAPLUS  
CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, dihydro-4-[(3R)-3-hydroxy-4-phenylbutyl]-2-oxo-, (4S)- (CA INDEX NAME)

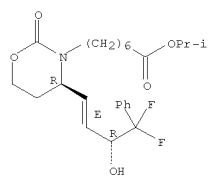
Absolute stereochemistry.



RN	768400-18-6	CAPLUS
CN	2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)	

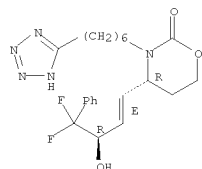
Absolute stereochemistry.  
Double bond geometry as shown.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 768400-21-1 CAPLUS  
 CN 2H-1,3-Oxazin-2-one,  
 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]tetrahydro-3-[6-(2H-tetrazol-5-yl)hexyl]-, (4R)- (CA INDEX NAME)

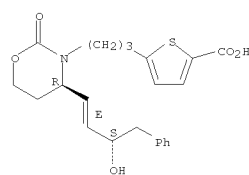
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 768400-26-6 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-dihydro-4-[(1E,3S)-3-hydroxy-4-phenyl-1-buten-1-yl]-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, (4R)- (CA INDEX NAME)

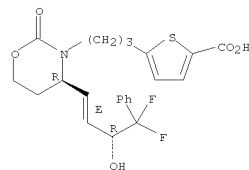
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



RN 768400-29-9 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, (4R)- (CA INDEX NAME)

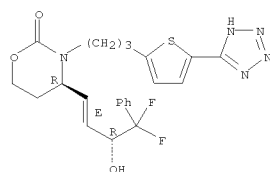
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 768400-32-4 CAPLUS  
 CN 2H-1,3-Oxazin-2-one,  
 4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]tetrahydro-3-[3-[5-(2H-tetrazol-5-yl)-2-thienyl]propyl]-, (4R)- (CA INDEX NAME)

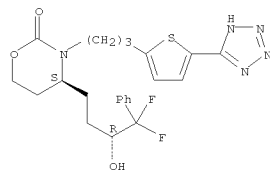
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



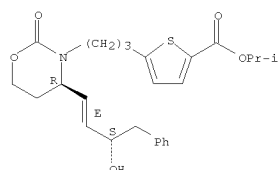
RN 768400-35-7 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 4-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]tetrahydro-3-[3-[5-(2H-tetrazol-5-yl)-2-thienyl]propyl]-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 768400-37-9 CAPLUS  
 CN 2-Thiophenecarboxylic acid, 5-[3-[(4R)-dihydro-4-[(1E,3S)-3-hydroxy-4-phenyl-1-buten-1-yl]-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

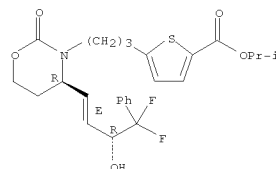
Absolute stereochemistry.  
 Double bond geometry as shown.



L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

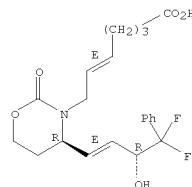
RN 768400-40-4 CAPLUS  
 CN 2-Thiophenecarboxylic acid,  
 5-[3-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]propyl]-, 1-methylethyl ester (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



RN 768400-43-7 CAPLUS  
 CN 5-Heptenoic acid, 7-[(4R)-4-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-buten-1-yl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]-, (5E)- (CA INDEX NAME)

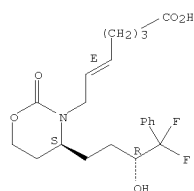
Absolute stereochemistry.  
 Double bond geometry as shown.



RN 768400-46-0 CAPLUS  
 CN 5-Heptenoic acid, 7-[(4S)-4-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]dihydro-2-oxo-2H-1,3-oxazin-3(4H)-yl]-, (5E)- (CA INDEX NAME)

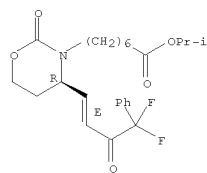
Absolute stereochemistry.  
 Double bond geometry as shown.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)



IT 768400-09-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of prostaglandin analogs as EP4 receptor agonists for the treatment of glaucoma)  
 RN 768400-09-5 CAPLUS  
 CN 2H-1,3-Oxazine-3(4H)-heptanoic acid, 4-[(1E)-4,4-difluoro-3-oxo-4-phenyl-1-buten-1-yl]dihydro-2-oxo-, 1-methylethyl ester, (4R)- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



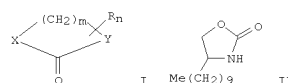
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1990:459177 CAPLUS  
 DOCUMENT NUMBER: 113:59177  
 ORIGINAL REFERENCE NO.: 113:10015a,10018a  
 TITLE: Preparation of oxazolidinone penetration enhancing compounds  
 INVENTOR(S): Rajadhyaksha, Vithal J.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 60 pp.  
 CODEN: FIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9000407	A1	19900125	WO 1989-US2779	19890623
W: JP				
RM: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4960771	A	19901002	US 1988-218316	19880712
EP 378657	A1	19900725	EP 1989-908033	19890623
EP 378657	B1	19940202		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03500298	T	19910124	JP 1989-507546	19890623
JP 2901297	B2	19990607		
AT 101046	T	19940215	AT 1989-908033	19890623
PRIORITY APPLN. INFO.:			US 1988-218316	A 19880712
			EP 1989-908033	A 19890623
			WO 1989-US2779	W 19890623

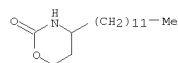
OTHER SOURCE(S): CASREACT 113:59177; MARPAT 113:59177  
 GI



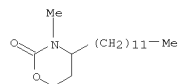
AB Title compds. I (R = H, C1-18 alkyl, cycloalkyl, aryl, aralkyl, alkoxy, etc.; X = O, R1N, R1 = H, alkyl, aralkyl, C1-18 acyl, cycloalkyl, etc.; Y = O, R2N, R2 = H, alkyl, aralkyl, cycloalkyl, C1-18 acyl, hydroxyalkyl, etc.; m = 2-4; n = 0-4, with several provisos) are prepared Me(CH2)9CHNH2CH2OH and ethylene carbonate were heated to .apprx.110° to give 4-decyloxazolidin-2-one (II). In a test using isosorbide dinitrate (0.07%) and 1.4% II, II showed superior permeation enhancing properties compared to control and a known permeation enhancer.  
 IT 128276-13-1 128276-14-2 128276-15-3

L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

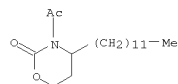
RL: RCT (Reactant); RACT (Reactant or reagent)  
 (penetration enhancer for topical pharmaceuticals)  
 RN 128276-13-1 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 4-dodecyltetrahydro- (CA INDEX NAME)



RN 128276-14-2 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 4-dodecyltetrahydro-3-methyl- (CA INDEX NAME)



RN 128276-15-3 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, 3-acetyl-4-dodecyltetrahydro- (CA INDEX NAME)

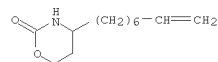


L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1990:407421 CAPLUS  
 DOCUMENT NUMBER: 113:7421  
 ORIGINAL REFERENCE NO.: 113:1417a,1420a  
 TITLE: Chemistry in adsorbed monolayers. 2. Thermal and photochemical grafting reactions at the polymer-filler interface  
 AUTHOR(S): McGarvey, Colette E.; Holden, David A.  
 CORPORATE SOURCE: Guelph-Waterloo Cent. Grad. Work Chem., Univ. Waterloo, Waterloo, ON, N2L 3G1, Can.  
 SOURCE: Langmuir (1990), 6(6), 1123-32  
 CODEN: LANGD5; ISSN: 0743-7463  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The photochem. of adsorbed long-chain  $\alpha$ -diazo ketones, azidoformates, and  $\alpha$ -azido ketones was examined as a method of coupling linear low-d. polyethylene with alumina, silica, and silica gel fillers. Photoreactions of monolayers adsorbed on alumina showed that grafting predominated and that interchain reactions were much less pronounced than analogous photoreactions in cyclohexane solution. Monofunctional coupling agents such as octadecanoyl azide provided no improvement in elongation at break, but bifunctional agents containing both a photochem. and a thermally active group, such as 12-azido-1-diazo-2-dodecanone and 1-diazo-11-dodecen-2-one, provided significant improvements. Evidence for improved adhesion between filler and polymer was provided by fracture-surface morphol. studies.

IT 126082-64-2P  
 RL: FORM (Formation, nonpreparative); PREP (Preparation)  
 (formation of, in photolysis of nitrogen-containing coupling agents)  
 RN 126082-64-2 CAPLUS  
 CN 2H-1,3-Oxazin-2-one, tetrahydro-4-(7-octenyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1974:14882 CAPLUS  
DOCUMENT NUMBER: 80:14882  
ORIGINAL REFERENCE NO.: 80:2497a,2500a  
TITLE: Cyclization of azidoformates  
AUTHOR(S): Breslow, David S.; Ward, George A.  
CORPORATE SOURCE: Res. Cent., Hercules Inc., Wilmington, DE, USA  
SOURCE: Journal of Organic Chemistry (1973), 38(24), 4205-6  
CODEN: JOCEAH; ISSN: 0022-3263  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The previously unidentified product (Breslow, D. S., et al., 1967) formed in the thermal decomposition of octadecyl azidoformate is 4-pentadecyltetrahydro-2H-1,3-oxazin-2-one. Thus, octadecyloxycarbonylnitrene "back-bites" to give both a five-membered and a six-membered ring compound. The compound reported previously as 4-methyltetrahydro-2H-1,3-oxazin-2-one is the 6-methyl derivative  
IT 42202-88-0P  
RL: SYN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 42202-88-0 CAPLUS  
CN 2H-1,3-Oxazin-2-one, tetrahydro-4-pentadecyl- (CA INDEX NAME)

